

2004

A Comparative Evaluation of the Cost Effectiveness of Treating the Metabolic Syndrome in African Americans and the General Population

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A Comparative Evaluation of the Cost Effectiveness of Treating the Metabolic Syndrome in African Americans and the General Population

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science

By

Joseph T. Tasosa, M.B.A.
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2004
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Dayton OH

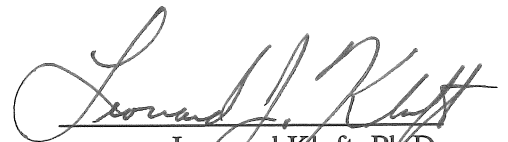
Wright State University
School of Graduate Studies
June 10, 2004

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY Joseph T. Tasosa ENTITLED A Comparative Evaluation of the Cost Effectiveness of Treating the Metabolic Syndrome in African Americans and the General Population BE ACCEPTED IN PARTIAL FULFILMENT FOR THE DEGREE OF Master of Science.

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ABSTRACT

Tasosa, Joseph T., M.B.A., Department of Social and Applied Economics, Wright State University, Dayton OH, 2004.

A Comparative Evaluation of the Cost Effectiveness of Treating the Metabolic Syndrome in African Americans and the General Population¹

¹The Metabolic Syndrome poses an important public health threat to the U.S. health care delivery system. Disparate access to quality health care makes African Americans (blacks) especially susceptible to the adverse effects of MS. Although direct evidence suggests that early treatment of MS risk factors saves lives, no study to date has compared the cost effectiveness of such measures in blacks and the general population. Interventions that promote early treatment of MS risk factors may improve public health but could also lead to excess costs that are ultimately borne by society. The objective of this study was to assess the value of early treatment of MS risk factors in blacks and the general population. A cost effectiveness analysis was carried out using a Markov decision model to compare early treatment and late treatment of MS risk factors in blacks and the general population. The main outcome measure was the incremental cost per Quality Adjusted Life Year (QALY). With the exception of early treatment of hyperlipidemia in blacks (\$187,462/QALY), early treatment of individual MS risk factors at age 30 was found to be cost effective (<\$27,000/QALY) for both blacks and the general population. With the exception of treatment of hyperlipidemia, early treatment strategies targeted at blacks were found to be more cost effective than those targeted towards the general population. Sensitivity analyses indicated that age and cost of treatment were the most influential factors in the model. The cost effectiveness of early treatment of MS risk factors in blacks and the general population compares favorably with similar health care interventions. The results support a growing body of literature that indicates the cost effectiveness of providing preventative services to apparently healthy individuals.

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Introduction

Metabolic Syndrome

The Metabolic Syndrome (MS) is a group of risk factors that are known to increase the incidence of cardiovascular and renal disease. These risk factors include abdominal obesity, insulin resistance, hypertension and dyslipidemia (Appendix A). The impairment of the fibrinolytic system and the presence of prothrombic and proinflammatory states have also been cited as important components of MS.

The National Health and Nutrition Examination Survey III (NHANES III, 1988-94) found 25% of all U.S. adults and 42% of those over the age of 60 have MS (Ford et al, 2002). Despite the high prevalence, there is still no generally accepted definition of MS (Scott, 2003). Most experts however, agree that the simultaneous presentation of three of the four major risk factors is sufficient for defining the MS (National Cholesterol Education Program Adult Treatment Panel III 2001 [NCEP ATP III], Meigs, 2002). For a more detailed discussion on the history and issues surrounding the definition of MS, see Appendix B.

Racial Disparities in Health care

Racial disparities in health care are described as "...racial or ethnic differences in the quality of health care that are not due to access related factors, clinical needs, preference, or appropriateness of intervention (Smedley et al [eds], 2003)." The Institute of Medicine (2003) views racial disparities in the context of the legal and regulatory climate of health care systems and in the context of stereotyping and prejudice.

As cited by Williams and Collins (1994), disparities in the provision of health care tend to diminish when socio-economic factors are held constant. Kitagawa and Hauser (1973) support this idea by documenting diminishing returns to health beyond a certain level of income. Similarly House et al (1993) conclude that income related health gains diminish for household incomes above \$20,000 per year.

While these assertions may be true for access related issues, Kressin and Petterson (2001) and Ofili (2000) argue

that racial disparities remain even after an adjustment for socio-economic status and other health care access related factors are accounted for.

The extent of health disparities in the African American (black) community has been extensively chronicled. Such documentation indicates race as an important factor in the diagnosis of MS risk factors. Blacks, for example, have a reduced chance of being diagnosed of some risk factors and therefore have a higher risk of cardiovascular disease than do whites (Brancati et al, 2000; Karter et al, 2002). As cited by Bell et al (2004), blacks are 1.97 times more likely to have untreated hypertension than are whites even after adjusting for socio-economic status.

Although racial and ethnic disparities in health care are consistent across a wide range of diseases and health care services (IOM, 2003), this study will focus on racial disparities as they relate to the MS. The purpose of this project is to study the economic cost of treating MS risk factors in blacks versus the general population.

General Population

New standards were announced in 1997 for the classification of individuals by race within the U.S. Federal Government's national data systems (Freid et al, 2003). These standards classified individuals under five main racial groups: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander and White. Race and Hispanic origin are considered as two separate and distinct concepts, thus Hispanics may be of any race. The general population in this study contains individuals from all five racial groups.

The purpose of this project is to study the economic cost of treating MS risk factors in blacks versus the general population at the national level thus national data was used. National data was also used because it is the most consistent and the most available.

Societal Perspective of Cost Effectiveness Analysis

Cost effectiveness analysis (CEA) is used by health consumers to assess the relative value of different health care services and by the health care industry to support

marketing claims. CEA is particularly useful when policy makers seek efficient policies but face certain constraints that prevent them from doing the more traditional Cost Benefit Analysis (Boardman et al, 2001). These constraints include the inability to capture all the social costs of an intervention (Gold et al, 1996). Social costs in our study measure the loss of economic productivity associated with MS outcomes.

Despite the importance, the loss of economic productivity was not factored into our CEA because it is difficult to quantify and could not be easily incorporated into our model. The QALY our measure of effectiveness has also been accused of not measuring social value because its preferences and weights are based on an individualistic perspective rather than a societal perspective (Drummond et al, 2000). Since it is society that ultimately bears the cost of health care, it would seem more appropriate if a more socially sensitive unit is used to measure cost and effectiveness. When all social costs are captured, the most allocatively efficient intervention becomes the most cost effective.

Methodology

Treatment Options and Clinical Outcomes

The progression path of the Metabolic Syndrome is illustrated through a Markov decision tree diagram (Fig. 1A and Fig. 1B) constructed using DATA 4.0 (TreeAge Software, Inc., Williamstown MA, USA). The model is able to simulate possible disease progression pathways by tracking a theoretical group of blacks and another of the general population at risk of the MS.

At the end of the simulation, the model calculates the number of people alive under each pathway and the costs involved. The Markov model is also able to estimate quality of life under each treatment option and the cost effectiveness per Quality Adjusted Life Year (QALY) gained (see Appendix B) as the groups move from one transition state to another.

Two treatment options were identified, (1) early treatment and (2) late treatment. We assume that MS risk

factors in the late treatment option go untreated until a major clinical outcome occurs. This is often the *status quo*. Stroke, Myocardial Infarction (heart attack) and End-Stage Renal Disease (ESRD) were chosen as the three major clinical outcomes of MS because they can be easily measured, they are the most prevalent and they are the most sensitive to intervention.

The impact of Stroke, Myocardial Infarction (MI) and ESRD can be reduced by early detection and treatment of the major components of MS (Lakka et al, 2003; Berg et al, 2001). Our hypothesis assumes that we can drastically reduce the negative impact of MS outcomes in blacks and the general population if we are able to provide early and aggressive treatment. This is especially important in the context of eliminating racial disparities in health care because reducing the negative impact of MS outcomes in blacks may lead to a reduction in racial disparities in health care.

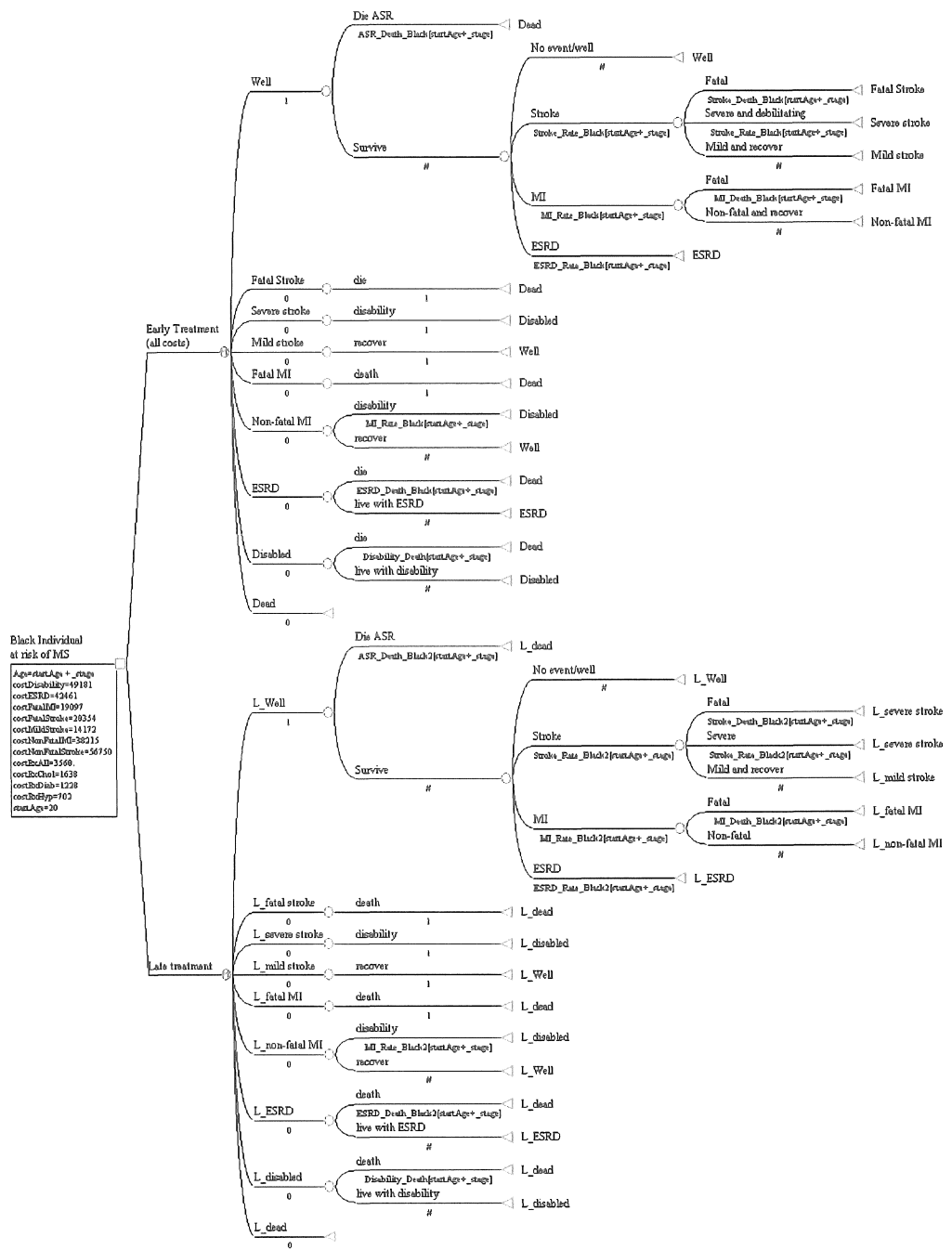


Fig 1A: Markov Decision Tree–African American

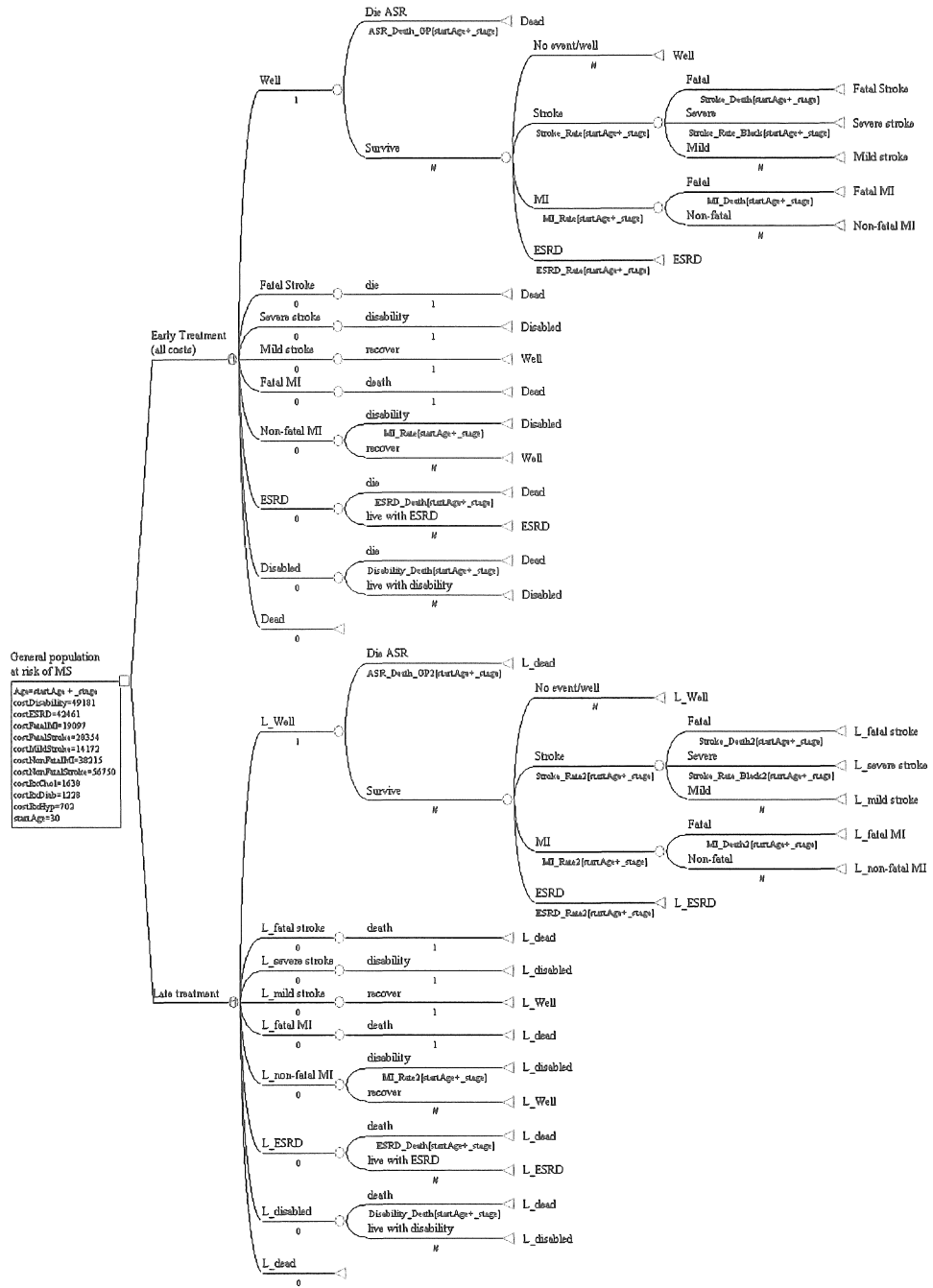


Fig 1B: Markov Decision Tree—General Population

Although the economic costs of providing early treatment are high, these costs may be offset by increased productivity and increased quality of life that arise from early treatment. In this study, the economic impact of treating MS risk factors in blacks is compared to that of treating the MS in the general population.

Subgroup Analysis

A target population may be separated into specific subgroups that are expected to exhibit a different level of effectiveness due to the intervention. Blacks are selected as a subgroup of the general population because they have different incidence and mortality rates. Although subgroup analysis may be relevant to the decision maker, its relevance must be weighed against the decreased precision of available data (Gold et al, 1996). Blacks are chosen as a subgroup because data on them is more readily available compared to other racial minorities.

Markov State Transition Model

Since some diseases and treatments are characterized by repetitive events, it becomes difficult for an analyst to portray this dynamic process in a static way (Drummond et al, 2000). The ability of the Markov model to represent repetitive events and its ability to accommodate the time dependence of both probabilities and utilities, allows it to more accurately represent clinical settings.

Markov models make the assumption that a patient is always in one of a finite number of health states also called Markov states. Events are represented as transitions from one Markov state to the other.

Markov models are useful when the timing of significant events is important and when these events are likely to happen more than once. Conventional decision trees are unable to accurately represent such clinical settings without over-simplifying model assumptions (Sonnenberg and Beck, 1993).

Markov Health States

Individuals in a cohort fall into one of the following definitive Markov states: (1) Well (2) Mild stroke, (3) Severe stroke, (4) Fatal stroke, (5) Non Fatal MI, (6) Fatal MI, (7) ESRD, (8) Disability and (9) Death.

The model is used to calculate the proportion of the cohort in each of the nine health states. The Markov model has a cycle time (the average amount of time spent in a health state) of one year and can only account for one transition between health states per year. A cycle time of one year is clinically meaningful even for rare events (Sonnenberg and Beck, 1993) but it can be shortened for more frequent events or for events that change rapidly (Goldman, 1983).

The model allows for persons to move from one state to another based on the transition probabilities of the two possible pathways. Transition probabilities help simulate the progression of groups through all possible combinations of events and outcomes over time. The type of event, the severity of the event and the age of an individual all influence the transition probabilities (Elliot et al,

2000). The severity of the event is in turn dependent upon a predetermined ratio of all possible outcomes of this event.

Individuals at the start of the simulation are assumed to be well. Individuals who recover completely can move back into the "well" state but individuals who become disabled or develop ESRD do not recover completely as these disease states are not regressive. A person in the well or disabled state may make a transition to the terminal death state. The death state (absorbing state) is the only state that a patient cannot leave. All the other states are temporary (See Fig. 2).

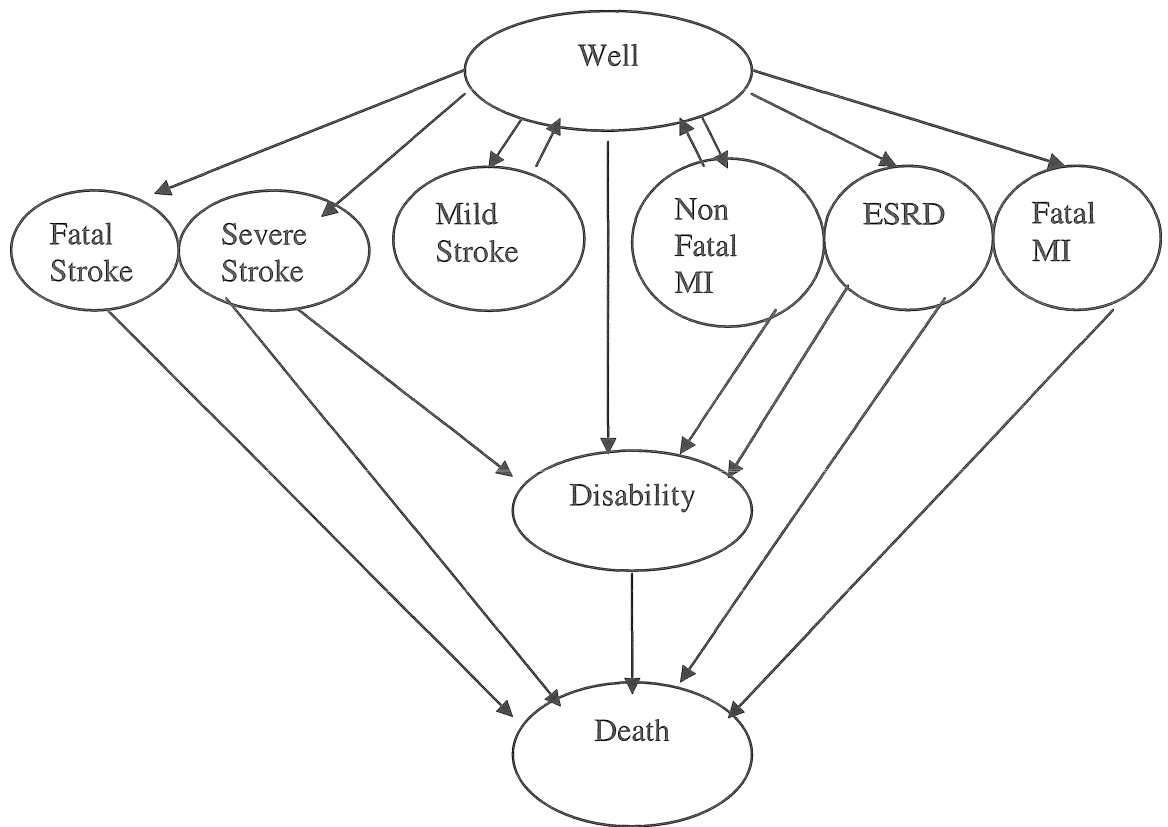


Fig. 2: Markov State Diagram. Each circle indicates a Markov state. Arrows indicate allowed transitions.

Medical Costs

Only intensive treatment costs of hypertension, hyperlipidemia and diabetes are used as these have the best effect in improving health. Costs are based on studies done by the CDC Diabetes Cost Effectiveness Group (1998, 2002) and expressed in 2004 US dollars discounted at an annual rate of 3% per year. A 3% social discount rate is based on recommendations by the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine (Gold et al, 1996: pp 233), on standard practice in economic evaluation (Weinstein and Stason, 1977; Brouwer and van Exel, 2004) and on related CEA studies (Busbee et al, 2003; Arguedas et al, 2004; Hoeger et al, 2004).

Costs of treating events are obtained from Elliot et al (2000). All costs are adjusted for inflation based on US Bureau of Labor Statistics inflation calculator and are listed in Table 1.

Table 1: Annual Costs of adverse events and treatment for
30 year old

Variable	Annual Value
Cost of Disability	\$49,181 ¹
Cost of ESRD	\$42,461 ¹
Cost of Fatal Myocardial Infarction	\$19,097 ¹
Cost of Fatal Stroke	\$28,354 ¹
Cost of Mild Stroke	\$14,172 ¹
Cost of Non fatal Myocardial Infarction	\$38,215 ¹
Cost of Non fatal Stroke	\$56,750 ¹
Cost of Hyperlipidemia Treatment	\$ 1,638 ³
Cost of Diabetes Treatment	\$ 1,228 ²
Cost of Hypertension Treatment	\$ 701 ²

¹ Elliot et al (2000)

² CDC Diabetes Cost-effectiveness Group

Prevalence Rates and Mortality Rates

The annual age related incidence of Stroke, MI, and ESRD are obtained from studies done by Williams (2001), U.S. Renal Data System (2003) and Wolf et al (1992) and are applicable to the general population.

Age specific mortality rates for the general population were estimated using 2000 U.S. life tables (Freid, et al, 2003) and these varied by race. As cited by (IOM, 2003) blacks have a 78% greater risk of mortality than the general population. Our assumption is that the excess mortality due to racial disparities in the provision of health care is 78% higher than that of the general population. Research also found the mortality rate of individuals with the MS to be twice as great as that of the average age, sex and race (ASR) adjusted mortality rate (Golan et al, 1999). These assumptions were incorporated into the life tables to estimate the impact of MS risk factors on mortality.

The adjusted hazard ratios for blacks (relative to that of whites) were 2.03 for ESRD (Karter et al, 2002) and

1.40 for Stroke (Pfizer, 2003). These hazard ratios were used to estimate the excess prevalence of ESRD and Stroke in blacks and the excess mortality in blacks due to ESRD and Stroke. Disability rates were derived from the US Social Security Database.

Although individuals with ESRD or disability are at an increased risk of having another event such as stroke or MI (Reaven et al, 1996), these effects have not been factored into the model, as literature on the event probabilities of such scenarios is not conclusive. We also know that individuals with multiple risk factors are at an increased risk of death than those without (Elliot et al, 2000). The synergistic effects of having multiple risk factors have however not been factored into the model.

Health Utilities

Health utilities are cardinal values that enable researchers to measure health related quality of life under conditions of uncertainty. Health utilities provide a means to quantitatively measure and compare two health states. The standard gamble approach, the time trade-off

approach, rating scales and the willingness to pay approach are some of the methods used to calculate health utilities (Petrou, 2003). For a brief discussion on the standard gamble approach see Appendix D.

Defining a set of health states is the first step in measuring health utilities. Each health state is assigned a utility value between 0 and 1 whose endpoints are death and perfect health. Our study uses utility values developed by Rizzo et al (1998) and CDC Diabetes Cost effectiveness Group (2002). Stroke is assigned a value of 0.5, MI 0.88, ESRD 0.61 and disability 0.46. These utility values are then used to estimate QALYs. Since health utilities are relative values, we can assume that they are affected by age, sex, culture, socio-economic status and race. The utility values used in this analysis however, are not race specific because such data is unavailable.

With the use of transition probabilities and utility of life measures associated with each treatment option, the model calculates the cost effectiveness of early treatment of MS in blacks and the general population. The simulation automatically terminates when individuals turn 77 or die.

Seventy-seven years is the life expectancy in the U.S. At the end of the simulation a group of 30 year olds was used as the base case to estimate parameters for both blacks and the general population.

Results

Base Case Analysis

Blacks

The incremental cost per QALY is the additional costs that early treatment imposes over late treatment for each QALY gained (*status quo*). Early treatment of hypertension, hyperlipidemia and diabetes together in 30-year-old blacks came at an estimated incremental cost of \$53,140/QALY gained. Early treatment of hyperlipidemia alone came at an estimated incremental cost of \$187,462/QALY gained, while early treatment of diabetes alone and hypertension alone came at an incremental cost of \$11,755 and \$2,456 per QALY gained respectively (Table 2A).

Table 2A: Cost/QALY Blacks

Age	All Three	Hyperlipidemia	Diabetes	Hypertension
20	78,816	121,393	19,939	7,612
30	53,140	187,462	11,755	2,456
40	36,363	517,696	5,396	**
50	23,259	*	224	**
60	14,840	*	**	**
70	11,879	316,337	**	**

* Late treatment dominated early treatment

** Early treatment dominated late treatment

Dominance

When choosing between two alternatives, we first apply the principle of strong dominance. One program is said to dominate another if its effectiveness were higher and its costs lower. In this case it is unnecessary to calculate a cost-effectiveness ratio (Gold et al, 196). As shown in Table 2A late treatment of hyperlipidemia in blacks dominated early treatment at age 50 and 60. The additional

cost of early treatment of hyperlipidemia is not met with any additional improvement in the quality of life of blacks at this age. It is therefore more cost effective to maintain the *status quo* and not to employ any early treatment strategies targeted towards blacks in this age group. Early treatment of diabetes in blacks dominated late treatment at age 60 and 70 and early treatment of hypertension dominated late treatment in blacks over the age of 40.

General population

Early treatment of hypertension, hyperlipidemia and diabetes together in a 30-year-old member of the general population came at an estimated incremental cost of \$63,926/QALY gained. Early treatment of hyperlipidemia alone came at an estimated incremental cost of \$26,243/QALY gained, while early treatment of diabetes alone and hypertension alone came at an incremental cost of \$17,789 and \$6,290 per QALY gained respectively (Table 2B).

With the exception of hyperlipidemia, the incremental cost per QALY gained by early treatment of MS risk factors was lower in blacks than it was in the general population. In general, this evidence suggests that early treatment of

MS risk factors in blacks is more cost effective than it is for the general population. Since we assume that blacks are more prone to the effects of MS than the general population, it follows that each additional dollar spent on preventative treatment of diabetes and hypertension in blacks saves more lives than each additional dollar spent on treating the same risk factors in the general population. The high cost of aggressive treatment of hyperlipidemia in blacks and the relatively low impact of this treatment however, makes it cost-ineffective relative to the general population.

Table 2B: Cost/QALY General Population

Age	All Three	Hyperlipidemia	Diabetes	Hypertension
20	94,414	39,168	27,599	12,355
30	63,926	26,243	17,789	6,290
40	41,084	16,291	10,240	**
50	25,412	8,852	4,602	**
60	16,662	4,641	1,741	**
70	14,213	4,059	2,051	**

** Early treatment dominated late treatment

When early treatment is more effective but less costly than late treatment, it is said to dominate. In our results early treatment of hypertension is dominant over late treatment for individuals over 40 (Table 2B). Individuals over 50 are the most prone to MS outcomes and so benefit the most from early treatment. Treating hypertension early may avoid the costly health problems it may cause if left untreated. As cited by the US Preventative Services Task Force, the complications due to hypertension are among the most common and most serious diseases in the U.S. Screening for hypertension is thus recommended for all children and adults.

Sensitivity Analysis

A one-way sensitivity analysis for the treatment of diabetes, hyperlipidemia and hypertension identified age and treatment costs as influential variables. The ranges used in the sensitivity analyses are specified in (Table 3).

Table 3: Variables Used in Sensitivity Analysis

Variable	Base-case	Range
Age	30	20-77
Treatment Cost (\$):		
Hypertension	702	282-822
Diabetes	1,228	1,092-1,364
Hyperlipidemia	1638	636-2,229

Varying the age

Treating MS risk factors in younger individuals was found to be more effective than treating the same risk factors in older individuals. This is because early detection of disease is associated with substantial increases in the quality of life. Although intensive treatment of MS risk factors is more effective for younger people, it came at an increased cost to society. Treating MS risk factors in younger individuals saved more lives than it did in older individuals. These results confirm our assumptions that preventive treatment strategies that start

early on in life are a more cost effective approach than are late treatment strategies. These data also complement studies that have shown that the majority of deaths below the age of 65 are preventable through interventions easily provided in a clinician's office (U.S. Preventive Services Task Force, 1996).

Treatment of hypertension, hyperlipidemia and diabetes together from age 20 resulted in 25 lives saved per year among blacks and 26 lives saved per year among the general population. The additional number of lives saved in the U.S. from age 20 to 70 dropped to 11.76 per year in blacks and to 12 per year in the general population. This was a drop of 53.6% in blacks and 53.8% in the general population.

Varying Costs

Increasing treatment costs decreased the cost effectiveness of treating MS risk factors. Conversely, reducing treatment costs resulted in a higher cost effectiveness. The incremental cost for the treatment of diabetes in blacks ranged between \$9,346/QALY and \$14,165/QALY, treatment of hypertension was between

\$2,190/QALY and \$4,582/QALY and treatment of hyperlipidemia between \$116,159/QALY and \$229,518/QALY.

The incremental cost for the treatment of diabetes in the general population ranged between \$23,685/QALY and \$31,513/QALY, treatment of hypertension was between \$140/QALY and \$8,880/QALY and treatment of hyperlipidemia between \$4,783/QALY and \$38,901/QALY. We did not attempt to do a sensitivity analysis for the treatment of all three risk factors because data on the appropriate limits is unavailable.

Discussion

Discounting is one of the prominent topics of debate in health economics as the idea that money today is worth more than money tomorrow also extends into health care analysis. Traditionally there have been two competing theories regarding the social discount rate: the social opportunity cost theory and the social rate of time preference theory (Drummond et al, 2000). While we have used a constant discount rate (social rate of time preference) of 3% in our analysis, this standard practice

by Weinstein and Stason (1977) has been criticized by some who argue that it does not fairly reflect a timeless societal preference for health and wealth, that is, individuals do not discount at constant rates (Cairns and van der Pol, 1996; Harvey, 1994, Brouwer and van Exel, 2004). Still others argue that there are differences between societal time preferences and individual time preferences (Olsen, 1993) and that costs and effects should be discounted at different rates (Gold et al, 1996).

While these arguments are compelling, we decided to follow the recommendations of the US Public Health Service Panel on Cost-Effectiveness in Health and Medicine (Gold et al, 1996). This expert panel argued that costs and effects should be discounted at a rate consistent with the shadow-price-of-capital approach to evaluating public investments. Given currently available data on real economic growth and given corresponding estimates of the real interest rate, the panel agreed that a rate of 3% would most closely estimate the real (riskless) discount rate for CEA.

Since CEA measures technical efficiency, rather than allocative efficiency it cannot easily indicate whether something is worth doing (Boardman et al, 2001). Hadley and

Holahan (2003) address this problem by choosing the annual cost it takes to treat ESRD as the *de facto* standard cost by which society in the U.S. is willing to pay for a health care intervention. Their assumption is based on the fact that MEDICARE, a federal health insurance program designed to provide health care for the elderly and the disabled also supports ESRD patients.

The incremental cost per QALY of most of the interventions in this study fall below the \$42,400/QALY it takes to treat an ESRD patient. This is true for the treatment of hyperlipidemia, diabetes and hypertension for all ages in the general population and for the treatment of diabetes and hypertension for all ages in blacks. The incremental cost per QALY was below \$42,400/QALY when all three MS risk factors were treated in blacks above 40 years. It was also below \$42,400/QALY when all three MS risk factors were treated in the general population above 50. It can be hypothesized that U.S. society is willing to pay for these interventions.

Early treatment of hypertension among blacks proved to be the most cost effective option. It is clear that mortality from several common and serious diseases can be

lowered through the detection and treatment of high blood pressure. As cited by Collins et al (1990), a reduction in diastolic BP by 5-6 mm Hg in hypertensive patients could reduce the incidence of coronary heart disease by 14% and incidence of strokes by 42%. Since blacks are especially prone to hypertension, its late treatment ultimately leads to massive increases in the health care costs borne by society.

Early treatment of hyperlipidemia in blacks proved to be the least cost effective option. This was because the high cost of aggressive treatment of hyperlipidemia did not result in a significant improvement in the quality of life among blacks. Our results complement recommendations set by the U.S. Preventive Task Force (1996), which found no sufficient benefits in routine screening of hyperlipidemia in children, adolescents, or young adults.

We found that at all ages and all costs in the general population, treatment of hypertension, hyperlipidemia and diabetes together was less cost effective than targeting a single risk factor. This is because the added cost in treating all three risk factors did not significantly improve the quality of life. In

general, screening for hypertension was the most cost effective option, followed by diabetes screening and hyperlipidemia screening.

The values estimated in this study compare favorably to federally mandated health care interventions. In a study that looked at the cost effectiveness of 587 public health care interventions in the U.S., Tengs et al (1996) found that the overall median intervention costs were about \$42,000/QALY. The median medical intervention cost was \$19,000/QALY; injury reduction \$48,000/QALY; and toxin control \$2,800,000/QALY.

Our results also compare well to cost effectiveness analyses carried out by Graham et al (1997) and Groeneveld et al (2001). Graham et al (1997) by looking at "The cost effectiveness of airbags by seating position," in a federally mandated program, demonstrated that driver side airbags have a cost effectiveness of \$30,000/QALY while passenger side airbags save lives at a cost of \$76,500/QALY. Groeneveld et al (2001) concluded that the incremental cost effectiveness of full Automated External Defibrillator deployment on commercial aircraft ranged

between \$ 35,300 and \$ 94,700 per QALY. Some major aircraft carriers have now deployed AED's in their aircraft.

Limitations

Although our economic analysis satisfied most of the criteria critical for a robust evaluation (Drummond et al, 2000; pp 27-51), we identified significant limitations.

The unavailability of reliable literature on the combined costs and effects of treating MS risk factors proved to be a big limitation. Although some studies have been performed to investigate the differences in MS event rates among the different races and ethnicities in the U.S., we are to our knowledge the first to compare the cost effectiveness of treating MS risk factors in blacks and the general population. Our study would have benefited had we been able to access similar studies and their associated data.

Another limitation is that our assumptions consider late term treatment as no treatment at all. This is not the case in the model as we have incorporated the effects

of moderate treatment into late treatment. Our decision to do this reflects our realization that, in reality, most at risk individuals do receive some sort of treatment over time and thus a strictly "no treatment" option is impractical. Accuracy in the analysis can be improved if late treatment is actually modeled as no treatment at all. This issue may be addressed by a sensitivity analysis that varies the costs of late treatment. Our initial study did not carry out this sensitivity analysis because we felt it would overly complicate our model.

The model assumes that patients in the early treatment group will follow an aggressive treatment regimen. The model does not allow for external factors such as non-compliance, discontinuation of treatment, adoption of other therapies or lifestyle adjustment. Lifestyle adjustments such as diet, physical inactivity, and nicotine and alcohol consumption play an important role in the manifestation of MS (Regenauer, 1996).

Our model does not incorporate clinical events that occur before diagnosis and assumes that individuals are in perfect health at the start of the treatment regimen. The model also assumes that treatment of MS begins at the onset

of the syndrome. In practice, individuals are not in perfect health at the start of treatment. In addition, treatment can only begin after clinical diagnosis.

One weakness of the Markov Model is that it requires rigid assumptions such as zero memory. With zero memory the transition probabilities depend only on the individual's current health state and not on prior events (Drummond et al, 2000; Beck and Pauker, 1983). If the model cannot refer to prior events in its analysis, it cannot adequately incorporate the interaction of risk factors over time.

Zero memory is a severe limitation because each of the MS components is known to be a risk factor for other conditions. As cited by Reaven et al (1996) and Zavaroni (1999), risk factors in combination, significantly increase the chance of developing potentially life-threatening illnesses such as ESRD, MI and stroke. Furthermore, having one component of MS increases your chances of having other components of the syndrome. The more components of MS one exhibits the greater is one's risk of CVD. Studies have indicated that men with three MS risk factors are nearly twice as likely to have a MI or stroke and more than three times more likely to develop heart disease than those with

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Appendices

Appendix A

Metabolic Syndrome

A person with at least three of the following cardiovascular risk factors is clinically diagnosed of having MS (NHANES ATP III):

- Abdominal obesity: waist circumference of > 102 cm (40 inches) in men and > 88 cm (35 inches) in women
- Hypertriglyceridemia: ≥ 150 mg/dL (1.69 mmol/L)
- Low High Density Lipoprotein (HDL) cholesterol: <40 mg/dL (1.04 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women
- High blood pressure: $\geq 130/85$ mm Hg
- High fasting glucose: ≥ 110 mg/dL (≥ 6.1 mmol/L)

Appendix B

Discussion on the Definition of MS

In the late 1960s, the MS was described as a "disorder of genetic adaptation becoming manifest following unrestricted food intake and/or muscular inactivity" (Hauner, 2002). The clustering of cardiovascular risk factors has since been given different names including Insulin Resistance Syndrome, Syndrome X, Dysmetabolic Syndrome, Multiple Metabolic Syndrome and Plurimetabolic Syndrome (Isoma et al, 2001 and Meigs, 2003). More recently MS has been called the "deadly quartet" to emphasize its high artherogenic potential (Hanefeld, Leonhardt and Kaplan; Hauner, 2002).

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Our belief is supported by an extensive study showing the prevalence of MS in the U.S. (Ford et al, 2002). Our belief is also supported by Gus et al (2004) who conclude that the risk of hypertension may be better identified by obesity defined by higher waist circumference than higher BMI. For these reasons, we adopt the NCEP ATP III definition of MS.

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Appendix C

Quality Adjusted Life Years

A QALY is a health index that estimates the quantity and quality of life generated by health care interventions. QALYs place weight on the time spent in different health states such that a year of perfect health is assigned a value of 1 and death is assigned a value of 0. Some health states are considered worse than death and are assigned negative scores (Thompson (2003)).

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Appendix D

Standard Gamble Approach

When calculating health utilities under the standard gamble approach (von Neumann and Morgenstern, 1953), an individual is presented with two choices: (1) the certainty of survival for a specific period of time in a particular state of health and (2) the gamble of survival for the same period of time without disability on one hand and with immediate death on the other. The chance of survival without disability, as opposed to the chance of death is varied until the individual is indifferent between certainty and gambling. This probability then estimates the utility of the individual for the disabled state (Petrou, 2003).

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between \$ 35,300 and \$ 94,700 per QALY. Some major aircraft carriers have now deployed AED's in their aircraft.

Limitations

Although our economic analysis satisfied most of the criteria critical for a robust evaluation (Drummond et al, 2000; pp 27-51), we identified significant limitations.

The unavailability of reliable literature on the combined costs and effects of treating MS risk factors proved to be a big limitation. Although some studies have been performed to investigate the differences in MS event rates among the different races and ethnicities in the U.S., we are to our knowledge the first to compare the cost effectiveness of treating MS risk factors in blacks and the general population. Our study would have benefited had we been able to access similar studies and their associated data.

Another limitation is that our assumptions consider late term treatment as no treatment at all. This is not the case in the model as we have incorporated the effects

of moderate treatment into late treatment. Our decision to do this reflects our realization that, in reality, most at risk individuals do receive some sort of treatment over time and thus a strictly "no treatment" option is impractical. Accuracy in the analysis can be improved if late treatment is actually modeled as no treatment at all. This issue may be addressed by a sensitivity analysis that varies the costs of late treatment. Our initial study did not carry out this sensitivity analysis because we felt it would overly complicate our model.

The model assumes that patients in the early treatment group will follow an aggressive treatment regimen. The model does not allow for external factors such as non-compliance, discontinuation of treatment, adoption of other therapies or lifestyle adjustment. Lifestyle adjustments such as diet, physical inactivity, and nicotine and alcohol consumption play an important role in the manifestation of MS (Regenauer, 1996).

Our model does not incorporate clinical events that occur before diagnosis and assumes that individuals are in perfect health at the start of the treatment regimen. The model also assumes that treatment of MS begins at the onset

of the syndrome. In practice, individuals are not in perfect health at the start of treatment. In addition, treatment can only begin after clinical diagnosis.

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